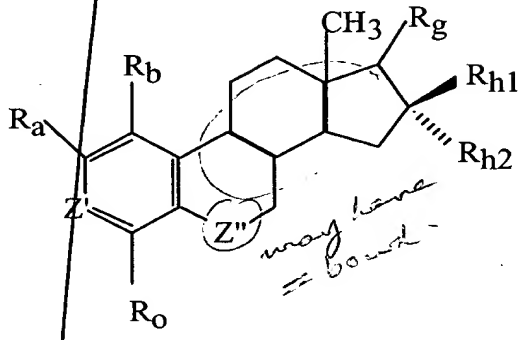
CLAIMS

We claim:

1. A compound of the general formula:



wherein:

a) R_b and R_o are independently -H, unless otherwise noted to be -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -OR_6, -CH_2-OH, -NH_2, or N(R_6)(R_7), wherein R_6 and R_7 are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons;

b) R_a is -N_3, -C≡N, -CH_2-C≡R, -C≡C-R, -C=CH-R, -R-C=CH_2, -C≡CH, -CH_2-C≡N, >C(H)-C(O)-OR_3, -O-R, -R-R_1, -O-R-R_1, OR(O)R, OR(O)R_1, ROR, ROR$_1$, -NHC(O)R_6, -NRC(O)R_6, -NH_2, or N(R_6)(R_7), wherein R_6 and R_7 are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons; or a hetero group wherein the hetero group may have more than one hetero atom and may be substituted, where R is H or a straight or branched alkyl with up to 10 carbons or aralkyl, and in any position F may be substituted in or on the carbon chain, and R_1 is -OH, -NH_2, -Cl, -Br, -I, -F or CF_3 when R_1 is terminal;

c) Z' is >COH, unless otherwise noted to be >C-OAc;

d) >C-Rg is >CH_2, >C(H)-OH, >C=O, >C=N-OH, >C(R_3)OH, >C=N-OR_3, >C(H)-NH_2, >C(H)-NHR_3, >C(H)-NR_3R_4, or >C(H)-C(O)-R_3, where each R_3 and R_4 is independently an alkyl or branched alkyl with up to 10 carbons or aralkyl; or

R_g is i) an alkyl of 1-10 carbon atoms that is straight chain or branched, ii) an alkenyl of 1-10 carbon atoms that is straight chain or branched having one or more double bonds at

any position from C to Zo, iii) an alkenyl group of 1-10 carbon atoms that is straight chain or branched having one or more triple bonds at any position where chemically possible, iv) a mono or dialkyl amino group wherein each alkyl chain has from 1-10 carbon atoms and is straight chain or branched, v) $(CH_2)_n$-CF_2-, $(CH_2)_n$-CR_1 or $(CH_2)_n$-CF_3 wherein n=0-10 carbons, or vi) H, and wherein any of i-iv are optionally substituted with an aromatic or heteroaromatic group or optionally substituted with a heterogroup and wherein Rg is either in the α or β position and; or

R_g is Rg_1 and Rg_2, and wherein Rg_1 may be present or absent and when present is –H, an alkyl, alkenyl, or alkynyl of 1-10 carbon atoms that is straight chain or branched and is optionally substituted, and Rg_2 is a hetero group, wherein when Rg_1 is absent the heterogroup is bonded to the 17-position with a double bond, and wherein either Rg_1 or Rg_2 can be in the β position with the other group in the α position, and R_1 is -OH, $-NH_2$, -Cl, -Br, -I, -F or CF_3 when R_1 is terminal;

e) R_{h1} and R_{h2} are independently H, unless otherwise noted to be a straight or branched chain alkyl, alkenyl or alkynyl with up to 10 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality that is either not substituted, mono-substituted or multiply substituted with an alkyl, alkenyl or alkynyl chain up to 10 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with at least one hetero, halo or alkyl; or R_{h1} and R_{h2} are independently a group containing at least one alphatic or aromatic group optionally substituted with at least one hetero, halo or alkyl;

f) Z" is $=CH_2$;

and wherein saturated bonds in any ring may be dehydrogenated;

and wherein all monosubstituted substituents have either an α or β configuration;

and wherein lower alkyl is defined as a carbon chain having 1-10 carbon atoms which may be branched or unbranched.

2. The compound of Claim 1, wherein :

R_a is $-OCH_3$; and

R_{g1} and R_{g2} are each H.

3. The compound of Claim 1, wherein :

R_a is $-OCH_3$; and

R_g is $=CH_2$.

4. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Rg_1 is absent; and
R_{g2} is =NOH.

5. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Rg_1 is β-H; and
R_{g2} is α-OH.

6. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Rg_1 is –H; and
R_{g2} is $-NH_2$.

7. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Z' is >C-OAc;
Rg_1 is -H; and
R_{g2} is -OAc.

8. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Rg_1 is –H; and
R_{g2} is $-CH_2CH_2CH_3$.

9. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
Rg_1 is –H; and
R_{g2} is $-CH_3$.

10. The compound of Claim 1, wherein :

R_a is -OCH_3; and

R_g is =$CHCH_2CH_3$.

11. The compound of Claim 1, wherein :

R_a is -OCH_3;

Rg_1 is –H; and

R_{g2} is -$NHCH_2CH_2CH_3$.

12. The compound of Claim 1, wherein :

R_a is -OCH_3; and

R_g is =$CHCH_3$.

13. The compound of Claim 1, wherein :

R_a is -OCH_3;

Rg_1 is –H; and

R_{g2} is -CH_2CH_3.

14. The compound of Claim 1, wherein :

R_a is -OCH_3; and

R_g is =N-NH-(SO_2)-C_6H_4-*p*-CH_3.

15. The compound of Claim 1, wherein :

R_a is –OCH_3;

R_g1 is H; and

R_g2 is -COOH.

Steps ?

16. A method of modifying estradiol analogs for preventing or hindering demethylation, oxidation and conjugation with another molecule during metabolism.

17. The method claim 16 wherein the method comprises adding steric bulk or modification of chemical or electrostatic characteristics or a combination thereof to estradiol analogs for retarding or preventing metabolic deactivation.

18. The compound of Claim 1, wherein:
R_a is $-OCH_3$;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and
R_{h1} and R_{h2} are independently -H and Et.

19. The compound of Claim 1, wherein:
R_a is $-OCH_3$;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and
R_{h1} and R_{h2} are independently H and n-Pr.

20. The compound of Claim 1, wherein:
R_a is $-OCH_3$;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and
R_{h1} and R_{h2} are independently H and i-Bu.

21. The compound of Claim 1, wherein:
R_a is $-OCH_3$;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and
R_{h1} and R_{h2} are independently H and CH_2OH.

22. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and
R_{h1} and R_{h2} are independently H and n-Bu.

23. The compound of Claim 1, wherein :

R_a is $-OCH_3$;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

Z" is $>CH_2$; and

R_{h1} and R_{h2} are independently H and Me.

24. The compound of Claim 1, wherein :

R_a is $-OCH_3$;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

R_{h1} and R_{h2} are independently H and $-CH_2N(CH_3)_2$.

25. The compound of Claim 1, wherein :

R_a is $-C(O)CH_3$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

26. The compound of Claim 1, wherein :

R_a is $-C(O)H$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

27. The compound of Claim 1, wherein :

R_a is $-CH_2OH$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

28. The compound of Claim 1, wherein :

R_a is $-NO_2$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

29. The compound of Claim 1, wherein :
R_a is $-N(CH_3)_2$;
$>C-R_{g1}$ is $>CH$; and
$>C-R_{g2}$ is $>COH$.

30. The compound of Claim 1, wherein :
R_a is $-NH_2$;
$>C-R_{g1}$ is $>CH$; and
$>C-R_{g2}$ is $>COH$.

31. The compound of Claim 1, wherein :
R_a is $-C\equiv C-CH_3$;
$>C-R_{g1}$ is $>CH$; and
$>C-R_{g2}$ is $>COH$.

32. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$;
$>C-R_{g1}$ is $>CH$; and
$>C-R_{g2}$ is $>COH$.

33. The compound of Claim 1, wherein :
R_a is $-CH_3$;
$>C-R_{g1}$ is $>CH$; and
$>C-R_{g2}$ is $>COH$.

34. The compound of Claim 1, wherein :
R_a is $-NH_2$; and
R_{g1} and R_{g2} are each H.

35. The compound of Claim 1, wherein :
R_a is $-C(O)NH_2$; and
R_{g1} and R_{g2} are each H.

36. The compound of Claim 1, wherein :
R_a is $-NH_2^+CH_3$; and
R_{g1} and R_{g2} are each H.

37. The compound of Claim 1, wherein :
R_a is $-N(CH_3)2$; and
R_{g1} and R_{g2} are each H.

38. The compound of Claim 1, wherein :
R_a is $-NH^+(CH_3)2$ (or $N(CH_3)2^{\bullet}HCl$); and
R_{g1} and R_{g2} are each H.

39. The compound of Claim 1, wherein :
R_a is $-NH^+(CH_3)2$ or $N(CH_3)2$-HCl; and
$>C-R_{g1}$ is >CH; and
$>C-R_{g2}$ is >COH.

40. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
$>C-R_{g1}$ is >CH;
$>C-R_{g2}$ is >COH; and
an olefin at C9-C11.

41. The compound of Claim 1, wherein :
R_a is $-OCH_2CH_3$;
R_{g1} is absent; and
R_{g2} is $=CHCH_3$.

42. The compound of Claim 1, wherein :
R_a is $-C\equiv C-CH_3$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

43. The compound of Claim 1, wherein :
R_a is $-C(O)H$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

44. The compound of Claim 1, wherein :
R_a is $-NHC(O)H$ or $-NNC(O)N$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

45. The compound of Claim 1, wherein :
R_a is $-CH_2OH$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

46. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

47. The compound of Claim 1, wherein :
R_a is $-CH_3$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

48. The compound of Claim 1, wherein :
R_a is $-CH=CHCH_3$;
R_g1 is absent; and
R_g2 $=CHCH_3$.

49. The compound of Claim 1, wherein :
R_a is $-OCH_2CH_3$;
R_g1 is absent; and
R_g2 $=CH_2$.

50. The compound of Claim 1, wherein :
R_a is $-C\equiv CCH_3$;
R_g1 is absent; and
R_g2 $=CH_2$.

51. The compound of Claim 1, wherein :
R_a is $-C(O)H$;
R_g1 is absent; and
R_g2 $=CH_2$.

52. The compound of Claim 1, wherein :
R_a is $-NHC(O)H$;
R_g1 is absent; and
R_g2 $=CH_2$.

53. The compound of Claim 1, wherein :
R_a is $-CH_2OH$;
R_g1 is absent; and
R_g2 $=CH_2$.

54. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$;
R_g1 is absent; and
R_g2 $=CH_2$.

55. The compound of Claim 1, wherein :
R_a is $-CH_3$;
R_g1 is absent; and
R_g2 $=CH_2$.

56. The compound of Claim 1, wherein :
R_a is $-CH=CHCH_3$;
R_g1 is absent; and
R_g2 $=CH_2$.

57. The compound of Claim 1, wherein :
R_a is $-OCH_2CH_3$; and
R_g1 and R_g2 are each H.

58. The compound of Claim 1, wherein :
R_a is $-C\equiv CCH_3$; and
R_g1 and R_g2 are each H.

59. The compound of Claim 1, wherein :
R_a is $-C(O)H$; and
R_g1 and R_g2 are each H.

60. The compound of Claim 1, wherein :
R_a is $-NHC(O)H$; and
R_g1 and R_g2 are each H.

61. The compound of Claim 1, wherein :
R_a is $-CH_2OH$; and
R_g1 and R_g2 are each H.

62. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$; and
R_g1 and R_g2 are each H.

63. The compound of Claim 1, wherein :
R_a is $-CH_3$; and
R_g1 and R_g2 are each H.

64. The compound of Claim 1, wherein :
R_a is $-CH=CHCH_3$; and
R_g1 and R_g2 are each H.

65. The compound of Claim 1, wherein :
R_a is $-OCH_2CH_3$;
R_g1 is H; and
R_g2 is CH_3.

66. The compound of Claim 1, wherein :
R_a is $-C\equiv CCH_3$;
R_g1 is H; and
R_g2 is CH_3.

67. The compound of Claim 1, wherein :
R_a is $-C(O)H$;
R_g1 is H; and
R_g2 is CH_3.

68. The compound of Claim 1, wherein :
R_a is –NHC(O);
R_g1 is H; and
R_g2 is CH_3.

69. The compound of Claim 1, wherein :
R_a is $–CH_2OH$;
R_g1 is H; and
R_g2 is CH_3.

70. The compound of Claim 1, wherein :
R_a is $–CH_2CH_3$;
R_g1 is H; and
R_g2 is CH_3.

71. The compound of Claim 1, wherein :
R_a is $–CH_3$;
R_g1 is H; and
R_g2 is CH_3.

72. The compound of Claim 1, wherein :
R_a is $–CH{=}CHCH_3$;
R_g1 is H; and
R_g2 is CH_3.

73. The compound of Claim 1, wherein :
R_a is $–OCH_2CH_3$;
R_g1 is H; and
R_g2 is CH_2CH_3.

74. The compound of Claim 1, wherein :
R_a is $-C\equiv CCH_3$;
R_g1 is H; and
R_g2 is CH_2CH_3.

75. The compound of Claim 1, wherein :
R_a is $-C(O)H$;
R_g1 is H; and
R_g2 is CH_2CH_3.

76. The compound of Claim 1, wherein :
R_a is $-NHC(O)H$;
R_g1 is H; and
R_g2 is CH_2CH_3.

77. The compound of Claim 1, wherein :
R_a is $-CH_2OH$;
R_g1 is H; and
R_g2 is CH_2CH_3.

78. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$;
R_g1 is H; and
R_g2 is CH_2CH_3.

79. The compound of Claim 1, wherein :
R_a is $-CH_3$;
R_g1 is H; and
R_g2 is CH_2CH_3.

80. The compound of Claim 1, wherein :
R_a is $-CH=CHCH_3$;
R_g1 is H; and
R_g2 is CH_2CH_3.

81. The compound of Claim 1, wherein :
R_a is $-OCH_2CH_3$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

82. The compound of Claim 1, wherein :
R_a is $-C\equiv CCH_3$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

83. The compound of Claim 1, wherein :
R_a is $-C(O)H$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

84. The compound of Claim 1, wherein :
R_a is $-NHC(O)H$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

85. The compound of Claim 1, wherein :
R_a is $-CH_2OH$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

86. The compound of Claim 1, wherein :
R_a is $-CH_2CH_3$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

87. The compound of Claim 1, wherein :
R_a is $-CH_3$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

88. The compound of Claim 1, wherein :
R_a is $-CH=CHCH_3$;
R_g1 is absent; and
R_g2 is $=CHCH_2CH_3$.

89. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
R_g1 is H; and
R_g2 is $-CH_2OH$.

90. The compound of Claim 1, wherein :
R_a is $-OCH_3$;
$>C-R_g1$ is $>CH$;
$>C-R_g2$ is $>COH$; and
an olefin at C6-C7.

91. The compound of Claim 1, wherein :
R_a is $-N_3$; and
$>C-R_g$ is $>CH$.

92. The compound of Claim 1, wherein :
R_a is $-H$; and
$>C-R_g$ is $>CH$.